IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/680,950	Confirmation No. 6033
Applicant	:	Robert Langley et al.	
Filed	:	October 8, 2003	
TC/A.U.	:	3761	
Examiner	:	DEAK, Leslie R	
For	:	METHODS AND DEVICES FOR PROCESSING BLOOD	
Docket No.	:	96-03	
Customer No.	:	23713	

CERTIFICATE OF ELECTRONIC MAILING

I hereby certify that this correspondence is being deposited with the United States Patent and Trademark Office electronically.

December 9, 2008 /michaelcurtis/
Date Michael Curtis

REPLY BRIEF

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

An appeal brief for this application was filed on August 7, 2008 appealing the rejections in the Final Office Action mailed January 18, 2008. This Reply Brief is in response to the Examiner's Answer mailed October 15, 2008.

III. STATUS OF CLAIMS

Claims 1-53 and 56-68 are pending in this application. Claims 54 and 55 have previously been canceled. By means of the Final Office Action issued on January 18, 2008, claims 1-53 and 56-68 were rejected and are presently appealed. The claims were last amended in the Amendment and Response filed on April 11, 2007.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. As restated in the Examiner's Answer of October 15, 2008, the Examiner rejects claims 1-12, 14-15, 17-40, 42-45, 47-50 and 67 under 35 U.S.C. §103(a) as being obvious over U.S. Patent 6,179,801 (herein referred to as "Holmes") in view of U.S. Patent 5,980,465 (herein referred to as "Elgas"). These rejections encompass the three independent claims of the application, claims 25-27.

The Examiner states that Holmes discloses a blood processing apparatus and method where patient data is entered into a control screen to calculate the blood donor's total blood volume. The total blood volume is used to determine various parameters of the apheresis procedure. Specifically, the Examiner asserts that the blood removal pump (reference number 1030) and blood return pump (reference number 1090) of Holmes are operated according to the predetermined operating protocol of the blood processing device, where the operating protocol operates, in part, on patient blood volume data (pages 3-4 of the Examiner's Answer). The Examiner admits that Holmes fails to disclose the steps of adjusting the blood removal flow rate and blood return flow rate during the blood processing procedure based on the total blood volume, but asserts that this deficiency is overcome by the combination with Elgas (page 4, lines 6-9, of the Examiner's Answer).

The Examiner states that Elgas discloses that maintaining a patient's total blood volume during extracorporeal procedures is clinically significant to the patient's physiological status, and teaches that increasing fluid flow to the patient in the event of a decrease in total blood volume is a good way to maintain the patient's status quo (page 4, lines 9-13, of the Examiner's Answer). The Examiner asserts that the disclosure in Elgas reasonably suggests that other steps, such as adjusting the blood withdrawal rate of the device, would be within the range of reasonable steps taken to maintain the patient's total blood volume (page 4, lines 13-19, of the Examiner's Answer). The Examiner concludes that it would have been obvious to one skilled in the

art to use the suggestion of Elgas, with regard to maintaining total blood volume through fluid flow rate adjustments, with the procedure in Holmes to arrive at the claimed invention.

2. With regard to claims drawn to "systemic" variations of the flow rates (claims 1, 11 and 23), the Examiner further asserts that Holmes clearly discloses that the apheresis system varies the flow rates based on a predetermined operating scheme. Since the apheresis system disclosed in Holmes controls such variations, the Examiner considers the flow rates adjusted by the apheresis system correspond to Applicants' "systemic" variations (page 5, lines 1-5, the Examiner's Answer).

3. With regard to claims 3, 8, 9 and 10, the Examiner states that Holmes discloses patient data, such as total blood volume, which is used to establish the operating parameters of the apheresis device (page 6, lines 10-13, of the Examiner's Answer). The Examiner then states that Holmes teaches that the volume transfer rate of blood flow is a variable based on a predetermined protocol of the apheresis device. Therefore, the Examiner concludes the blood flow rate is a result-effective variable under MPEP 2144.05. The Examiner states that the optimization of a result-effective variable involves only routine skill in the art, and considers the variable flow rates in the present claims (e.g., increasing, decreasing, exponentially decreasing, or linearly varying) to be a result-effective variable, the adjustment of which does not patentably distinguish over the prior art of record (page 6, lines 13-25, of the Examiner's Answer).

4. With regards to claims 4-7, 30-31 and 34-39, the Examiner notes that the blood flow rates in these claims are based on specific equations. As discussed above, the Examiner asserts that Holmes discloses that the flow rate is recognized to be a result-effective variable (page 7, lines 1-3, of the Examiner's Answer). The Examiner states that absent a disclosure that Applicant's claimed equations provide a significant advantage over the prior art's calculation, the Examiner considers the selection of such variable parameters to be mere optimization of a result-effective variable through

routine experimentation under MPEP 2144.05 (page 7, lines 3-12, of the Examiner's Answer).

5. As restated in the Examiner's Answer, the Examiner also rejects claims 59-62 and 68 under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas, further in view of U.S. Patent 6,730,054 (herein referred to as "Pierce"). Pierce describes a blood processing procedure and device where blood is removed from a donor, recirculated through the device, and the desired blood components separated and collected.

With regards to claims 59-62 and 68, which disclose specific equations for determining the proper blood fraction for collection based, in part, on cycle duration and the hematocrit ratio between the removed blood and recirculated blood, the Examiner states that each portion of blood necessarily has a hematocrit value, and that the draw and return cycles of Holmes and Pierce have a rate. The Examiner concludes that all of the values used in the equations are demonstrated by the prior art to be variable and concludes these claims are therefore merely the optimization of a result-effective variable under MPEP 2144.05 (page 12, line 14, through page 13, line 5, of the Examiner's Answer).

VII. ARGUMENTS

Applicants appeal the rejections raised in the Final Office Action of January 18, 2008 for the reasons set forth in the Appeal Brief of August 7, 2008. This Reply Brief is in response to certain arguments raised in the Examiner's Answer of October 15, 2008 and is meant to supplement the arguments made in the Appeal Brief.

Claims 1-12, 14-15, 17-40, 42-45, 47-50 and 67 rejected under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas

This ground of rejection encompasses independent claims 25-27, which recite methods of processing blood comprising removing blood from a subject at a selected removal flow rate and returning at least a portion of the blood to the subject at a selected return flow rate, wherein the blood removal flow rate and/or return flow rate are adjusted during operation of the blood processing procedure based on the subject's total blood volume. Applicants believe the Examiner has failed to make a proper prima facie case of obviousness based on Holmes in combination with Elgas.

The Examiner states that the blood removal pump and blood return pump (reference numbers 1030 and 1090) of Holmes are operated according to a predetermined operating protocol of the blood processing device, where the operating protocol operates, in part, on patient blood volume data (pages 3-4 of the Examiner's Answer). With regard to the combination with Elgas, the Examiner states that Elgas discloses that maintaining a patient's total blood volume during extracorporeal procedures is clinically significant to the patient's physiological status and that increasing fluid flow to the patient in the event of a decrease in total blood volume is a good way to maintain the patient's status quo (page 4, lines 9-13, of the Examiner's Answer). The Examiner asserts that Elgas reasonably suggests that other steps, such as adjusting the blood withdrawal rate of the device, would be within the range of

reasonable steps taken to maintain the patient's total blood volume (page 4, lines 13-19, of the Examiner's Answer). The Examiner concludes that it would have been obvious to one skilled in the art to use the suggestion of Elgas, with regard to maintaining total blood volume through fluid flow rate adjustments, with the procedure in Holmes to arrive at the claimed invention. Applicants respectfully disagree.

In the response to arguments presented in the Appeal Brief of August 7, 2008, the Examiner maintains that Holmes discloses using patient parameters to calculate total patient blood volume, which is then used to determine various parameters of the apheresis procedure, such as blood inlet rate and outlet rate (page 13, lines 12-21, of the Examiner's Answer). Accordingly, it is the position of the Examiner that Holmes teaches a method in which the blood inlet and outlet rates are determined by various parameters, including blood volume. As such, the Examiner asserts that Holmes teaches adjustable flow rates and the importance of total blood volume (page 13, line 18, through page 14, line 4, of the Examiner's Answer).

However, it should be emphasized that while Holmes does state that total blood volume can be used to determine various parameters of the device and to estimate the number of blood components to be collected (column 56, line 61, to column 57, line 2 of Holmes), there is no disclosure that the parameters associated with total blood volume are related to the protocols involving the blood removal pump or blood return pump. In short, there is no teaching in Holmes that total blood volume is utilized to adjust blood removal rate or return rate.

Additionally, it should be emphasized that the problem in Elgas is a loss of blood volume in the patient, such as traumatic bleeding during surgery. The solution taught in Elgas is to add an outside fluid, such as a blood transfusion or IV fluid, to replace the blood lost during surgery. There is no disclosure in Elgas to address the patient's blood loss by adjusting the blood return rate or removal rate of the device. To support the combination of Holmes and Elgas, the Examiner appears to be taking the position that adding a new fluid from an outside source to replace the lost blood volume is

substantially the same as adjusting the blood removal rate or return rate of the device itself. However, this is not the case. Merely adjusting the blood removal rate or return rate of the device would not replace the lost blood and would be insufficient to correct the problem presented in Elgas.

The Examiner states that blood is withdrawn and returned to and from the device in Elgas via a variable-speed roller pump (item 22 in Elgas), which suggests the adjustability of flow rates (page 14, lines 11-13, of the Examiner's Answer). However, as pointed out in the Appeal Brief, the variable-speed roller pump 22 referenced by the Examiner is not used to withdraw blood from the patient, but is used to move blood from the reservoir 20 to the oxygenation unit 24 after the blood has already been removed from the patient (column 2, lines 44-47, of Elgas). Instead, the fluid in the patient's circulatory system is diverted from the vena cava by catheter 18 and sucked from the patient's chest cavity by a cardiotomy pump 17 through a cardiotomy filter 19 into the reservoir 20 (column 2, lines 40-44, of Elgas). In response, the Examiner asserts that if the reservoir comprises a closed container, when it is empty, the pump will create a vacuum in the direction of the inlet lines, thereby allowing adjustments in the speed of the pump affecting blood withdrawal rates (page 15, lines 6-11, of the Examiner's Answer). However, this is speculation on part of the Examiner. There is no disclosure in Elgas that the variable-speed roller pump 22 is used to adjust the withdrawal rate, or that it would even be capable of having an appreciable effect on the withdrawal rate. Additionally, such an assumption ignores the function of the cardiotomy pump 17 which is described by Elgas as being responsible for removing the blood from the patient.

The Examiner further asserts that it naturally follows that if a patient's blood volume changes, one using the device in Elgas would adjust the variable-speed roller pump 22 to adjust the blood withdrawal and return rates (page 14, lines 15-20, of the Examiner's Answer). As discussed above, the assumption that the variable-speed roller pump 22 adjusts the blood withdrawal rate of the device is not supported by Elgas. Additionally, if the patient in Elgas has a change in total blood volume, such as blood loss during surgery, adjusting the blood removal rate or return rate of the device would

not replace the lost blood volume. Since the device in Elgas is a heart-lung machine which oxygenates the blood for the patient during the surgery, significantly adjusting the withdrawal rate or return rate of the heart-lung machine could be catastrophic to the patient. The Examiner further states that Elgas is being used to illustrate the criticality of patient blood volume and that adjusting fluid flow rates is a recognized way of responding to changes in the blood volume (page 14, lines 18-20, of the Examiner's Answer). However, the problem raised in Elgas is how to respond to changes, particularly drastic decreases, in blood volume. This is the opposite of the present invention and Holmes where the patient's blood volume remains substantially constant and no significant adjustment of total blood volume is made. Accordingly, it would not be obvious for skilled in the art to combine the teachings of Elgas with Holmes to arrive at the present invention.

For these reasons, Applicants maintain their assertion that the Examiner has failed to make a proper prima facie case of obviousness in light of Holmes in combination with the suggestion provided by Elgas, and appeal this ground of rejection.

Claims 1, 11 and 23 drawn to "systematically" varying the flow rates

With regard to claims drawn to "systemic" variations of the flow rates (claims 1, 11 and 23), the Examiner asserts that Holmes clearly discloses that the apheresis system varies the flow rates based on a predetermined operating scheme. Since the apheresis system disclosed in Holmes controls such variations, the Examiner considers the flow rates adjusted by the apheresis system correspond to Applicants' "systemic" variations (page 5, lines 1-5, the Examiner's Answer). In the Appeal Brief and previous responses, Applicant argued that the term "systemically varying" as defined in the specification refers to substantially linear, exponential, logarithmic, or quadratic variations. In response, the Examiner argued that the use of the term "may be" in the definition is open ended, indicating that other variations are permissible within the

definition of "systematically varying" (page 16, line 16, through page 17, line 4, of the Examiner's Answer).

Applicants' argument that the definition of "systematically varied" refers to substantially linear variations, exponential variations, logarithmic variations, or quadratic variations has been raised in responses since the Response filed December 11, 2006. The Examiner has not responded to this argument until the recent Examiner's Answer of October 15, 2008. Page 19 of the specification states, "In the present invention, parameters such as return flow rate, removal flow rate, return time, removal time, the fraction of removed blood collected or recirculated may be systematically varied by substantially linear variations, exponential variations, logarithmic variations, quadratic variations." The term "may be" refers to the fact that the return flow rate, removal flow rate, return time, and removal time may be systematically varied or may not be systematically varied. Applicants believe that this language, especially in light of the comments made of record, supports the definition that the term "systemically varying" refers to substantially linear, exponential, logarithmic, or quadratic variations. Holmes does not teach making substantially linear, exponential, logarithmic, or quadratic variations; therefore it believed this rejection should be withdrawn.

Further grounds of rejection for claims 3, 8, 9 and 10 as well as 4-7, 30-31 and 34-39

Claims 3, 8, 9 and 10 ultimately depend from independent claim 27. Taken with the limitations of claim 27, these claims recite that the blood return flow rate decreases over the return time, decreases exponentially, decreases substantially in an exponential manner, or increases over the return time based on the determined total blood volume. Claims 4-7, 30-31 and 34-39 ultimately depend from independent claim 27 and recite blood return flow rates and removal flow rates adjusted according to specific equations. The Examiner asserts that the variable flow rates and equations in the present claims are result-effective variables under MPEP 2144.05 making these claims mere

optimization of a result-effective variable (page 6, line 10, through page 7, line 12, of the Examiner's Answer).

In the Appeal Brief, Applicants argued that adjusting blood return rate and blood removal rate based on total blood volume has not been recognized as a result-effective variable. MPEP 2144.05 requires that:

> "A particular parameter must first be recognized as a result effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of such variable might be characterized as routine experimentation. In re Antoine, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)"

In response, the Examiner argues that Elgas discloses adjustment of patient blood volume through administration of blood transfusions or IV fluids, but also asserts that the variable-speed roller pump (item 22) of Elgas removes blood from the patient, suggesting that fluid removal rate may also be used to control patient blood volume. In response to Applicants' argument that the variable-speed roller pump 22 does not remove blood from the patient, the Examiner states that if the reservoir comprises a closed container, the pump will create a vacuum in the direction of the inlet lines allowing adjustments to the blood withdrawal rates. The Examiner then argues that taken together, Holmes and Elgas reasonably suggest that manipulation of blood removal or return rates are result-effective variables that, when manipulated, control the patient's total blood volume (page 17, lines 6-16, of the Examiner's Answer).

As discussed above, there is no disclosure in Elgas that the variable-speed roller pump 22 is used to adjust the withdrawal rate. Additionally, this assumption ignores the teaching in Elgas that the cardiotomy pump 17 is what removes the blood from the patient (column 2, lines 40-44, of Elgas). Without this assumption, there is no suggestion in Elgas that the blood removal rate may be used to adjust the patient's total blood volume. Furthermore, blood removal rate and return rate are not used to achieve a desired total blood volume in Holmes or the present claims. Instead, the total blood volume remains substantially constant in the present invention and is used to adjust the flow rates to maintain proper pressure in the accessed blood vessel. While Holmes

discloses that total blood volume can be used to determine various parameters of the device, there is no disclosure that the parameters associated with total blood volume are related to the protocols involving the blood removal rate or blood return rate. Accordingly, there is no recognition in Holmes or Elgas, or in combination, that the blood return rate and removal rate can be beneficially varied according to total blood volume of the patient.

Under MPEP 2144.05, the prior art must recognize the process and the importance of the variable within the process. The examiner has not cited any evidence that the prior art recognizes the importance or criticality of adjusting the blood removal rate or return rate based on the total blood volume for the claimed process or any other process involving blood apheresis. Thus, total blood volume has not been recognized as a result effective variable which achieves a recognized result in the present claims and the requirements of MPEP 2144.05 have not been met. Further, the prior art does not teach or suggest the specific equations recited in claims 4-7, 30-31 and 34-39. Therefore, a proper prima facie case for obvious has not been made and these rejections should be withdrawn.

Rejection of claims 59-62 and 68 under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas, further in view of Pierce

The Examiner also rejects claims 59-62 and 68 under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas, further in view of Pierce. Pierce describes a blood processing procedure and device where blood is removed from a donor, recirculated through the device, and the desired blood components separated and collected.

With regards to claims 59-62 and 68, which disclose specific equations for determining the proper blood fraction for collection based, in part, on cycle duration and the hematocrit ratio between the removed blood and recirculated blood, the Examiner

states that each portion of blood necessarily has a hematocrit value, and that the draw and return cycles of Holmes and Pierce have a certain rate. The Examiner concludes that all of the values used in the equations are demonstrated by the prior art to be variable and concludes these claims are therefore merely the optimization of a result-effective variable under MPEP 2144.05 (page 12, line 14, through page 13, line 5, of the Examiner's Answer). In response to Applicants' arguments in the Appeal Brief, the Examiner states that Pierce teaches that hematocrit values are calculated based on flow considerations (column 7, lines 14-20). The Examiner concludes that variation of flow conditions, including the duration of the draw and return cycles, necessarily varies the hematocrit values, creating a result-effective variable (pages 18-19 of the Examiner's Answer).

As stated above, MPEP 2144.05 requires a parameter must be recognized as a result-effective variable which achieves a recognized result before the determination of the optimum or workable ranges of such variable can be characterized as routine experimentation. Claims 59-62 and 68 involve multiple variables all of which must interact in a specific manner to meet the limitations of the claims. For example, claims 59-62 and 68 utilize variables such as a first and second rate (R_1 and R_2) of blood flow, the ratio of the removed blood hematocrit with the recirculated blood hematocrit, and the duration of the draw cycle and return cycle in order to generate the collected blood fraction (F_{cmax}). While each of these may be recognized in the art as variables, the prior art has not recognized that the ratio of the removed blood hematocrit and recirculated blood hematocrit as modified by cycle duration times and as further modified by the rate of blood flow during the cycles can be utilized to select the blood fraction (by volume) that the desired blood component is to be collected from. Accordingly, the requirements of MPEP 2144.05 have not been met and this ground of rejection should be withdrawn.

Conclusion

For the reasons above and previously presented in the Appeals Brief, a decision withdrawing the pending rejections and allowing the pending claims is therefore respectfully requested.

This Reply Brief does not contain any new or non-admitted amendments, affidavits or other evidence. It is believed no fee is required with this submission. If this is incorrect, please deduct from Deposit Account No. 07-1969 the appropriate fee for this submission and any extension of time required.

Respectfully submitted,

/michaelcurtis/

Michael Curtis
Reg. No. 54,053

GREENLEE, WINNER AND SULLIVAN, P.C.
4875 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone (303) 499-8080
Facsimile: (303) 499-8089
Email: winner@greenwin.com
Attorney Docket No.: 96-03